

Applicants: Hendrik Sibolt Van Damme et al.

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Amendments to the Claims:

Please amend Claims 1, 3, 6-8, 13-17, 22, 24, 27 and 31, and add new Claims 33-34 as set forth below.

1. (Currently amended) A method for screening of cellular responses of cells or cellular components comprising:

(a) providing cells or cellular components on the surface of a solid porous metallo-oxide substrate, wherein said cells or cellular components are mammalian cells, insect cells, yeast cells, fungal cells, plant cells, bacteria, viruses or components thereof, and wherein

(i) said solid porous substrate has oriented through-going channels;  
(ii) said solid porous substrate retains said cells or cellular components on its surface, and wherein,

(iii) said solid porous substrate has immobilized therein, within the pores, an array of detector molecules, wherein said detector molecules are nucleic acids, peptides, proteins, antibodies, antibody fragments, enzyme substrates or specific dyes and wherein said detector molecules are appropriate to detect cellular responses to be assayed;

(b) delivering test compounds to positions on the substrate corresponding to the arrayed detector molecules on the surface of said solid porous substrate;

(c) incubating said test compounds with said cells or cellular components on the surface of the solid porous substrate, under conditions allowing the induction of cellular responses, wherein said cellular responses are chemically-induced or physiological events in said cells; production, secretion or surface exposure of a molecule of interest by said cells; membrane surface molecule activation; receptor activation; transmembrane ion transports; or transcriptional

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regulations;

(d) assaying said cellular responses, wherein cellular responses are detected using said detector molecules; and,  
identifying and characterizing the cellular responses induced by said test compounds.

2. (Original) The method according to claim 1, wherein said solid substrate is a flow-through porous solid substrate.

3. (Currently amended) The method according to claim 1, wherein said providing of cells or cellular components on the surface of a substrate is by a deposit directly on said substrate of an inoculum or a culture.

4. (Previously presented) The method according to claim 1, wherein said delivering of test compounds is by means of contact force.

5. (Original) The method according to claim 4, wherein said contact force is a capillary force or a piezo-electric-force.

6. (Currently amended) The method according to claim 1, wherein the nutrient(s) are provided from underneath the pores of the solid surface.

7. (Currently amended) A method for screening of cellular responses of cells or cellular components comprising:  
(a) providing cells or cellular components on the surface of a solid porous metallocide substrate, wherein said cells or cellular components are mammalian

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cells, insect cells, yeast cells, fungal cells, plant cells, bacteria, viruses or components thereof, and wherein

- (i) said solid porous substrate has oriented through-going channels, and
- (ii) said solid porous substrate retains said cells or cellular components on its surface;
- (b) incubating test compounds with said cells or cellular components on the surface of the solid porous substrate, under conditions allowing the induction of cellular responses, wherein said cellular responses are chemically-induced or physiological events in said cells; production, secretion or surface exposure of a molecule of interest by said cells; membrane surface molecule activation; receptor activation; transmembrane ion transports; or transcriptional regulations; and
- (c) assaying said cellular responses by
  - (i) providing a detector molecule to the cells or cellular components;
  - (ii) washing off excess of unincorporated detector molecule; and
  - (iii) detecting the presence or absence of a change in a detectable signal from the detector molecule, the presence of a change in detectable signal indicating a cellular response; wherein said detector molecule is a nucleic acid, peptide, protein, antibody, antibody fragment, enzyme substrate or specific dye.

~~The method according to claim 1, wherein said assaying of cellular responses is by:~~

- (a) ~~providing a detection agent to the cellular components;~~
- (b) ~~washing off excess of unincorporated detecting agent; and~~
- (c) ~~detecting the presence or absence of a change in detectable signal, the presence of a change in detectable signal indicating a cellular response.~~

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8. (Currently amended) The method according to claim 1, wherein said cellular response is assayed in whole broth or cell culture medium, in isolated cells such as pelleted cells, in supernatant of the cells or cellular components, or in lysate of the cells cellular components.
9. (Previously presented) The method according to claim 1, wherein said delivery of test compounds is by a means chosen from the group comprising a delivery mask, a high precision x-y-z pipettor, inkjet printer, and manual handling.
10. (Original) The method according to claim 9, wherein said delivery of test compounds is by means of a high precision x-y-z pipettor or inkjet printer.
11. (Previously presented) The method according to claim 1, wherein said identifying of the cellular responses is by luminescence.
12. (Original) The method according to claim 11, wherein said luminescence is fluorescence.
13. (Currently amended) The method according to claim 1, wherein said cellular components are ~~selected from the group consisting of mammalian cells, insect cells, yeast cells, fungal cells, plant cells, microbial cells, bacterial cells, cellular vesicles or [[,]] cellular organelles, tissue sections, and whole organisms including nematodes.~~
14. (Currently amended) The method according to claim 1, wherein said detector molecules are ~~selected from the group consisting of nucleic acids including~~

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~~modified analogues thereof, peptides, proteins, antibodies, antibody fragments, enzyme substrates and specific dyes.~~

15. (Currently amended) The method according to claim 1, wherein said cellular responses are ~~chosen from the group consisting of~~ chemically induced or physiological events in the cell ~~including selected from the group consisting of~~ lysis, apoptosis, growth inhibition, and growth promotion; ~~production, secretion, and surface exposure of a protein or other molecule of interest by the cell; membrane surface molecule activation including receptor activation; transmembrane ion transports; and transcriptional regulations.~~
16. (Currently amended) The method according to claim 1, 15, wherein said molecule of interest is selected from the group consisting of peptides, lipopeptides, glycosylated peptides, ~~antimicrobial peptides~~, polypeptides, proteins, enzymes, antimicrobial molecules, and primary and secondary metabolites, ~~and small organic molecules including pharmaceutical molecules.~~
17. (Currently amended) The method according to claim 1, wherein said test compound is a drug or a ~~any~~ compound which is useful in the selection process of a drug candidate.
18. (Original) The method according to claim 17, wherein said test compound is a drug selected from a chemical or natural drug candidate library.
19. (Previously presented) The method according to claim 1, wherein said solid substrate is an aluminum-oxide substrate.

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20. (Previously presented) The method according to claim 1, wherein said assaying is performed in real-time.
21. (Previously presented) The method according to claim 1, wherein said assaying is an end-point assaying.
22. (Currently amended) The method according to claim 7, wherein said providing a detector molecule detection agent to the cells or cellular components occurs prior to delivering of test compound thereby providing pre-labeled cells or cellular components.
23. (Previously presented) The method of claim 1, wherein an induced cellular response of a host cell is monitored.
24. (Currently amended) The method of claim 1, wherein cells or cellular components are provided using on-chip recombination, transformation or viral introduction.
25. (Previously presented) The method of claim 1, comprising assaying host cells with test compounds.
26. (Previously presented) The method of claim 1, wherein an array of detector molecules is provided within the pores of said substrate, and wherein an array of test compounds is provided within predefined regions, wherein said test compounds are in liquid solution and not immobilized in the substrate.

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27. (Currently amended) The method of claim 1, wherein an array of detector molecules is provided within the pores of said substrate, and wherein an array of cells or cellular components is provided in predefined regions on a substrate, said cells or cellular components being conditioned for preservation on said substrate.
28. (Previously presented) The method of claim 1, wherein an array of detector molecules is provided within the pores of said substrate, and wherein a cellular component is provided on a substrate, said cellular component being conditioned for preservation on said substrate.
29. (Previously presented) The method according to any of claims 26 to 28, wherein said array of detector molecules comprises a plurality of equal detector molecules or a plurality of different detector molecules.
30. (Previously presented) The method according to claim 27 or 28, wherein said condition is chosen from the group comprising lyophilization and glycerol dissolution.
31. (Currently amended) The method according to claim 1, wherein the cells or cellular components on the surface of the substrate comprise cells or cellular components with low spreading properties.
32. (Canceled)
33. (New) The method according to claim 1, wherein said cells or cellular are bacterial cells or components thereof.

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34. (New) The method of claim 1, wherein said test compounds are small organic molecules or pharmaceutical molecules.